REMARKS

STATUS OF THE CLAIMS.

Claims 45-70 and 74-76 are pending with entry of this amendment. Claims 45-67 are allowed. Claim 68 is amended herein. Support for the amendment to claim 68 is found in Applicants' specification at least at page 89, line 19 - page 90, line 2. Specifically, claim 68 has been amended to recite the detection of an amplification "of unique sequences from ~~at least one chromosomal region, wherein said~~ the chromosomal region ~~is~~ on chromosome 17, position q22 to position q24, wherein the unique sequences comprise a target polynucleotide sequence hybridizable with a probe specific for chromosome 17, q22 to q24." Applicants' specification describes the detection of an amplification at 17q22-24 by comparative genomic hybridization (CGH), which was confirmed by fluorescence in situ hybridization (FISH) using a probe specific for the 17q22-q24 region. The amendment therefore introduces no new matter.

The amendment to claim 68 makes an acknowledged distinction over the cited art more explicit. Accordingly, Applicants believe that this amendment resolves all outstanding issues and raises no new ones. Under 37 C.F.R. § 1.116, amendments to the claims after final rejection may be entered if the amendments place the claims in better form for consideration on appeal. Applicants submit that the above amendment meets this criterion. The amendment is necessary to more clearly recite Applicants' invention. The amendment was not presented earlier because the need for the amendment was not apparent until the Final Office Action was received. Entry of the amendment is thus permitted under § 1.116 and is respectfully requested.

35 U.S.C. §102.

Claims 68, 69, 74, and 75 were rejected under 35 U.S.C. § 102 as allegedly anticipated by Lavialle et al. (Anticancer Research (1989) 9:1265-1280). Office Action, page 1. This rejection is respectfully traversed.

Of the rejected claims, only claim 68 is independent. Claim 68 relates to a method for detecting a copy number variation in a suspected breast cancer sample by detecting an amplification of unique sequences from position q22 to position q24 on chromosome 17. Detection is carried out by hybridizing a suitable probe to the sample and detecting the hybridization complex.

> In explaining the rejection, the Examiner stated:
>
> Lavialle teaches [a] method for detecting a copy number variation in a suspected breast cancer sample (see page 1267, figure 1, page 1266, column 2 and page 1269, column 1, line 5) on chromosome 17, from position q22 to position q24 (page 1269, column 1, lines 3-6, where Lavialle states "However, in this case, cells without DMs still have a high level of c-myc amplification (30 fold) and the c-myc copies are integrated into an ABR at 17q24."

Office Action, page 2. Thus, Lavialle teaches an amplification of c-myc sequences. C-myc sequences are from 8q24. Applicants' specification, page 34, line 10. In Lavialle's cells, amplified c-myc sequences were translocated from 8q24 to 17q24. Lavialle teaches nothing with respect to the sequences normally present at 17q24, i.e., "hybridizable with a probe specific for chromosome 17, q22 to q24." Therefore, Lavialle fails to teach or suggest that an amplification of unique sequences from position q22 to position q24 on chromosome 17 is associated with anything, much less a breast cancer sample.

By contrast, Applicants demonstrated that the amplification detected at 17q22-24 was an amplification of sequences normally present in this region. More specifically, Applicants' specification describes a fluorescence in situ hybridization (FISH) study using a probe specific for the 17q22-24 region, which confirmed that the amplification observed was of sequences from this region. Applicants' specification, page 89, line 19 - page 90, line 2. Thus, Applicants' specification, and not Lavialle, teaches that an amplification of unique sequences from position q22 to position q24 on chromosome 17 is associated with breast cancer. While Lavialle might arguably suggest detecting an amplification of 8q24 (c-myc) sequences in a suspected breast cancer sample, nothing in Lavialle teaches or suggests detecting an amplification of 17q22-24 sequences in such a sample.

The Office Action makes it clear that the Examiner understands the above-described distinction over Lavialle. *See* Office Action, page 5. The Examiner stated, for example:

> Applicant attempts to amend the claim by parsing a difference between the word "at" and the word "from". In particular, Applicant argues that the amplification of Lavialle may be "at" 17q22-24, but that the amplified c-myc sequences were "from" 8q24.

Id. at page 5. The Examiner found Applicants' argument unpersuasive because the Examiner believed that the previous claims did not adequately capture this distinction. *Id.* at pages 5-6. The Examiner cited three bases for this position.

First, the Examiner noted that "in the patient sample that Lavialle uses, the [amplified] c-Myc sequences are 'from' 17q22-24," despite the fact that c-myc sequences are normally present at 8q24, and thus Lavialle detected amplified 8q24 sequences. Claim 68 has been amended to recite that the amplified sequences "comprise a target polynucleotide sequence hybridizable with a probe specific for chromosome 17, q22 to q24." Office Action, page 6. Lavialle's amplified sequences do not meet this criterion: a probe ***specific for*** 17q22-24 would, by definition, not hybridize to 8q24 sequences.

Second, the Examiner stated:

> Applicant appears to wish that the 17q22-24 region be limited to nucleic acids which are originally from 17q22-24, rather than ones like c-myc that are translocated to that region. However to the extent that specific structure exists, none is implied by the claim.

Id. As amended, claim 68 now defines the amplified sequences as comprising "a target polynucleotide sequence hybridizable with a probe specific for chromosome 17, q22 to q24." As one skilled in the art readily appreciates, "a probe specific for chromosome 17, q22 to q24" refers to a probe specific for sequences ***normally***, or in the Examiner's parlance, ***originally*** present in 17q22-24. Since claim 68 requires that the amplified sequences comprise sequences hybridizable with a probe specific for sequences normally present at 17q22-24, amended claim 68 clearly recites the structural element that the Examiner found lacking in previously pending claim 68.

Third, according to the Examiner, "the argument that sequences 'normally present' at 17q22-24 are not detected by Lavialle demonstrates Applicant's intention to read limitations into the claims (which are likely not supported by the specification)." *Id.* Applicants respectfully submit that one skilled in the art would not share the view that the specification fails to describe the amplification of sequences normally present at 17q22-24. Applicants confirmed the amplification of such sequences using a probe specific for 17q22-24. Those skilled in the art understand that such a probe specifically hybridizes to sequences that normally reside in this region. Probes specific for a particular locus are widely used to identify sequences "from" or "normally present" at that locus, regardless of whether the sequences are found at the locus, or somewhere else in the genome, in the sample being tested. As Applicants used an art-recognized hybridization method to demonstrate that amplification of 17q22-24 sequences, the specification provides unequivocal support for amplification of sequences normally present at 17q22-24.

Claims 69, 74, and 75 depend from claim 68 and are therefore novel over Lavialle for at least the same reason. Withdrawal of the § 102 rejection of claims 68, 69, 74, and 75 is therefore respectfully requested.

35 U.S.C. §103(A).

Claims 70 and 76 were rejected under 35 U.S.C. § 103(a) as allegedly obvious in light of Lavialle in view of Mullis *et al.* (U.S. Patent No. 4,683,202) Office Action, page 3. This rejection is respectfully traversed.

Claims 70 and 76 depend from claim 68 and therefore incorporate the element of detecting an amplification of 17q22-24 sequences. The Examiner contended that Lavialle teaches the detection of amplifications in this region. However, as explained above, Lavialle fails to teach or suggest the detection of an amplification of "a target polynucleotide sequence hybridizable with a probe specific for chromosome 17, q22 to q24," as recited in amended claim 68.

Mullis does nothing to remedy this deficiency. Mullis is cited as teaching the elements recited in claims 70 and 76, namely labeling the sample nucleic acid (claim 70) and using cDNA as the sample nucleic acid (claim 76). *See* Office Action, page 5. Mullis neither teaches nor suggests anything about detecting a copy number variation in a suspected breast cancer sample by detecting an amplification of 17q22-24 as recited in claim 68 and incorporated into dependent claims 70 and 76. Thus, the Lavialle-Mullis combination fails to teach or suggest all of the elements of rejected claims 70 and 76. Withdrawal of the § 103 rejection of these claims over Lavialle and Mullis is therefore respectfully requested.

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Should the Examiner form the intention to maintain the rejections, Applicants request a telephone interview with the Examiner prior to the issuance of another Office Action.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 769-3509.

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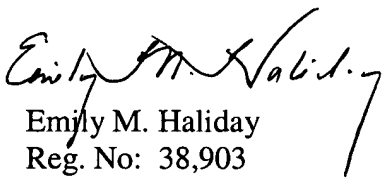
Respectfully submitted,



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